EFFECT OF VEHICLES AND SODIUM LAURYL SULPHATE ON XENOBIOTIC PERMEABILITY AND STRATUM CORNEUM PARTITIONING IN PORCINE SKIN

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ABSTRACT

Dermal contact with potentially toxic agricultural and industrial chemicals is a common hazard encountered in occupational, accidental spill and environmental contamination scenarios. Different solvents and chemical mixtures may influence dermal absorption. The effects of sodium lauryl sulphate (SLS) on the stratum corneum partitioning and permeability in porcine skin of 10 agricultural and industrial chemicals in water, ethanol and propylene glycol were investigated. The chemicals were phenol, *p*-nitrophenol, pentachlorophenol, methyl parathion, ethyl parathion, chlorpyrifos, fenthion, simazine, atrazine and propazine. SLS decreased partitioning into stratum corneum from water for lipophilic compounds, decreased partitioning from propylene glycol and did not alter partitioning from ethanol. SLS effects on permeability were less consistent, but generally decreased permeability from water, increased permeability from ethanol and had an inconsistent effect on permeability from propylene glycol. It was concluded that, for the compounds tested, partitioning into the stratum corneum was determined by the relative solubility of the solute in the donor solvent and the stratum corneum lipids. Permeability, however, reflected the result of successive, complex processes and was not predictable from stratum corneum partitioning alone. Addition of SLS to solvents altered partitioning and absorption characteristics across a range of compounds, which indicates that partition coefficients or skin permeability from neat chemical exposure should be used with caution in risk assessment procedures for chemical mixtures.

Keywords: Skin permeability; Dermal absorption; Stratum corneum partitioning; Water; Ethanol; Propylene glycol; Phenol; *p*-Nitrophenol; Pentachlorophenol; Methyl parathion; Ethyl parathion; Chlorpyrifos; Fenthion; Simazine; Atrazine; Propazine

Abbreviations: SLS, Sodium Lauryl Sulphate; CMC, Critical Micelle Concentration; log Ko/W, log of the octanol/water partitioning ratio

INTRODUCTION

Dermal contact with potentially toxic agricultural and industrial chemicals is a common hazard encountered in occupational, accidental spill and environmental contamination scenarios. The risk of toxicity is related to the ability of these compounds to reach the site of toxic effect. This usually involves dermal penetration and absorption, unless the skin surface is the site of toxicity. Since chemicals may be encountered in a variety of solvents, solvent mixtures and chemical mixtures; the effects of solvents and chemicals in the mixture on the dermal kinetics of the chemical of interest is relevant. Most current dermal risk assessment guidelines only deal with single chemical exposure. The large variety of solvents and chemical mixtures that may be encountered prohibits the empirical characterization of the dermal kinetics of all possible mixtures. However, certain mixture-effects may be reasonably predicted from studies on the effects of similar mixtures on similar compounds.

The outer layer of the skin, the stratum corneum, is generally accepted to be the primary barrier to skin absorption for most compounds (Bouwstra et al 2003) and the intercellular lipid matrix of the stratum corneum is the main route for the dermal absorption of chemicals (Albery & Hadgraft 1979). Absorption through intact stratum corneum usually involves two processes—partitioning into the stratum corneum and movement through the lipid matrix (Scheuplein & Blank 1971). Mixture effects on the rate and extent of either of these processes will conceivably influence the rate and extent of dermal absorption.

Effects on dermal absorption rates have been demonstrated using a variety of surfactants, including sodium lauryl sulphate (SLS) (Frankild et al 1995; Effendy et al 1996; Baynes & Riviere 1998; Lopez et al 2000; Nielsen 2000; Riviere et al 2001; Shokri et al 2001; Baynes et al 2002; Nokhodchi et al 2003). Surfactants may change skin barrier properties by causing skin irritation (Lee & Maibach 2004). If present above the critical micelle concentration (CMC), reversible, altered structural organization of stratum corneum lipids may occur. Surfactants can also reduce the amount of chemical available for absorption through the formation of micelles in the donor solvent. Different, and occasionally apparently contradictory, surfactant influences on dermal absorption may be encountered depending on the interplay between the various surfactant effects (Riviere et al 2001; Shokri et al 2001; Baynes et al 2002).

Water, ethanol and propylene glycol are common solvents and their effects on dermal absorption across a range of compounds have been described (Berner et al 1989; Kurihara-Bergstrom et al 1990; Megrab et al 1995; Kim et al 1996; Levang et al 1999; Panchagnula et al 2001). Comparing the dermal absorption of a range of compounds from these solvents with and without the addition of SLS offers an opportunity to study SLS effects on absorption when in combination with solvents relevant to a significant number of real-world dermal exposure hazards. SLS is common in mixtures associated with skin exposure. It is included in chemical formulations as emulsifiers, stabilizers and wetting agents (Shokri et al 2001) in products such as pharmaceutical vehicles, cosmetics, foaming dentifrices and foods (Nikitakis et al 1991). In this study, 10 representative agricultural and industrial compounds, chosen to characterize a range of physical properties, were used to investigate the effects of SLS on partitioning into isolated porcine stratum corneum and permeability in dermatomed porcine skin from water, ethanol and propylene glycol.

MATERIALS AND METHODS

Chemicals

C-14 radio labeled phenol, *p*-nitrophenol, pentachlorophenol, methyl parathion, ethyl parathion, atrazine, and simazine were obtained from Sigma (St. Louis, MO). Chlorpyrifos, fenthion, and propazine were obtained from American Radiolabeled Chemicals (St. Louis, MO). Purity ranged from 95 to 99. 5% and radioactivity ranged from 9 to 76.6 mCi/mmol. All C-14 labels were situated in the ring structure of the labeled molecules. Pure ethanol was obtained from Aaper Alcohol and Chemical Co. (Shelbville, KY). Sodium lauryl sulphate (99%; GC Grade), Bovine serum albumin (Fract V; cold alcohol precipitated), NaCL (Certified A.C.S.), KCl (Certified A.C.S.), CaCl (Certified A.C.S.; anhydrous), KH_2PO_4 (Certified A.C.S.), $MgSO_4$–$7H_2O$ (Certified A.C.S.), $NaHCO_3$ (Certified A.C.S.) and dextrose (Certified A.C.S.; anhydrous) was obtained from Fisher Scientific (Pittsburgh, PA). Pure propylene glycol was obtained from Sigma (St. Louis, MO). Amikacin (250 μg/ml) was obtained from Abbott Labs (Chicago, IL). Heparin (1000 units/ml) was obtained from Elkins Sinn (Cherry Hill, NY). Penicillin G Sodium (250,000 units/ml) was obtained from Pfizer Inc. (New York, NY).

Stratum corneum/solvent partitioning

Stratum corneum/solvent partition coefficients were estimated using methods described previously (Baynes 2000). Briefly, abdominal skin of female weanling Yorkshire pigs was immersed in 0.25% trypsin (Sigma, St. Louis, MO) for 24 h. The stratum corneum was then removed after heat treatment, dried in a Fisherbrand Dessicator Cabinet (Fisher Scientific, Pittsburgh, PA) with Drierite™ anhydrous calcium sulfate (WA Hammond Drierite Company, Xenia, OH), weighed (5–8 mg per sample) using a Mettler AE 200 scale (Mettler Toledo, Columbus, OH) and placed in vials. The solvent (3 ml), and 100 μg radio labeled compound was added to the stratum corneum sample vial (n = 5) and capped for 24 h. Then 250 μl of the solvent was removed for direct radiolabel counts using Ecolume (ICN Costa Mesa, CA). Excess solvent was removed from the stratum corneum by gentle blotting on Kimwipe™. The stratum corneum samples were combusted in a Packard Model 306 Tissue Oxidizer (Packard Chemical Co., Downers Grove, IL). Samples were analyzed using a Packard Model 1900TR Liquid Scintillation Counter (Packard Chemical Co., Downers Grove, IL).

It should be noted that SLS could not be dissolved directly into ethanol and propylene glycol. SLS, as a 40% mass/mass aqueous solution, was added to the solvents at a ratio of 25% (v/v). This resulted in 10% (m/v) SLS in the SLS-containing mixtures.

Permeability

Porcine skin disks, dermatomed from fresh skin to a thickness of 500 μm and presenting an exposed surface of 0.32 cm^2, were used as barrier membranes in a flow-through diffusion cell system according to the methodology of (Bronaugh & Stewart 1985), as adapted by (Chang & Riviere 1991). The dose volume was 20 μl. The target dose was 10 $\mu g/cm^2$. Actual doses, as estimated from the dosing stock solutions, were influenced by solvent interactions and non-specific binding with glassware. Doses used, followed by their standard errors in brackets were: 10.34 $\mu g/cm^2$ (0.24) for methyl parathion, 15.15 $\mu g/cm^2$ (0.33) for ethyl parathion, 5.69 $\mu g/cm^2$ (0.13) for chlorpyrifos, 5.93 $\mu g/cm^2$ (0.06) for fenthion, 7.89 $\mu g/cm^2$ (0.06) for phenol, 13.71 $\mu g/cm^2$ (0.05) for *p*-nitrophenol, 13.43 $\mu g/cm^2$ (0.16) for pentachlorophenol, 8.61 $\mu g/cm^2$ (0.03) for atrazine, 6.87 $\mu g/cm^2$ (0.08) for simazine and 10.69 $\mu g/cm^2$ (0.14) for propazine. The receptor solution, designed to mimic a blood plasma environment, consisted of 13.78 g NaCL, 0.71 g KCl, 0.56 g CaCl, 0.32 g KH_2PO_4, 0.58 g $MgSO_4$–$7H_2O$,

5.50 g $NaHCO_3$, 2.40 g dextrose, 90.0 g bovine serum albumin, 0.25 ml amikacin, 10 ml heparin and 0.1 ml penicillin G sodium made up to 2 l with glass distilled water. An 8 h experimental period was used, which allowed the estimation of adequate flux/time curves while avoiding complications due to skin degradation. Constant perfusate flow provided infinite sink conditions, maintaining a concentration gradient across the membrane. Perfusate was collected at 15 min intervals for the first 2 h, and 1 h intervals thereafter ($n = 5$). Radiolabel in the perfusate was determined by liquid scintillation as described above for solvents.

Data processing and statistical analysis

For partition coefficient determinations, radioactivity content in the vehicle mixture and stratum corneum were normalized to 1000 mg vehicle ($C_{vehicle}$) and 1000 mg stratum corneum ($C_{stratum\ corneum}$), respectively. The log stratum corneum/vehicle partition coefficient was determined from the equation: log PC = log $C_{stratum\ corneum}/C_{vehicle}$. The log K octanol/water values were obtained from the literature (Howard & Meylan 1997).

For permeability estimations the receptor fluid was assumed to be an infinite sink because of the constant flow of receptor fluid out of the diffusion cell. Permeability (cm/hr) was estimated by dividing the slope of the steady-state portion of the cumulative mass absorbed/time curve with the concentration in the donor solvent.

Differences between means were assumed to be statistically significant at or above the 95% confidence level as determined by *t* distribution tests assuming normal population variable distributions. The research adhered to the 'Principles of Laboratory Animal Care' (NIH publication #85–23, revised 1985).

RESULTS

Stratum corneum/solvent partitioning

Partitioning estimations were summarized in Table 1. The partitioning into stratum corneum from water of phenol and *p*-nitrophenol, which have relatively low log Ko/w values of 1.46 and 1.91, respectively, was not altered by the addition of SLS. For compounds with higher log Ko/w values, except simazine, partitioning was reduced when SLS was added (Figure 1). Partitioning from water increased as compound log Ko/w values

increased and log Ko/w was correlated with log $_{P\text{stratum corneum/solvent}}$ (R^2 = 0.7915). The addition of SLS to water removed the influence of compound log Ko/w values on stratum corneum partitioning (Figure 1).

Addition of SLS to ethanol did not alter stratum corneum/solvent partitioning except for simazine, which showed an increased partitioning and ethyl parathion, which showed decreased partitioning. Partitioning was weakly correlated with log Ko/w in both ethanol and ethanol-SLS mixtures (Figure 2).

Addition of SLS to propylene glycol reduced stratum corneum/solvent partitioning for atrazine, methyl parathion and pentachlorophenol. Ethyl parathion, fenthion and chlorpyrifos partitioning appeared to be reduced, but it was not statistically significant. It may, however, be reasonable to assume that *p*-nitrophenol partitioning was reduced, because it narrowly fell outside the chosen statistical significance level of 95% (*P*-value = 0.061). Simazine showed an increased partitioning. Phenol partitioning appeared to be unchanged. Partitioning was weakly correlated with log Ko/w in both propylene glycol and propylene glycol-SLS mixtures (Figure 3).

Permeability

Permeability estimations were summarized in Table 2. Permeability from propylene glycol was generally lower than permeability from water or ethanol (Table 2). The effects of SLS on permeability from water, ethanol and propylene glycol was summarized in terms of the ratio of permeability from solvents with SLS to solvents without SLS (Figure 4). The flux/time estimations of phenol were presented in (Figure 8) as a representative plot to illustrate typical flux/time curves obtained. Permeability estimation values were tabulated in Table 2. SLS generally reduced permeability from water except for phenol, which did not show significant change when SLS was present. SLS generally increased permeability from ethanol, except for ethyl parathion. SLS increased permeability from propylene glycol for phenol, *p*-nitrophenol, simazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol, but permeability was decreased for atrazine and methyl parathion. SLS did not change permeability for propazine.

The relationships between partitioning and permeability was represented in Figure 5, Figure 4.6 and Figure 7. The flux/time curves estimated for phenol was displayed as a representative curve to demonstrate typical flux/time curves (Figure 8).

DISCUSSION

These results are of interest in the field of risk assessment, because such mixture-studies have not been conducted for this wide variety of chemicals. It offered the opportunity to observe mixture-effects that are relevant across a range of compounds, which adds confidence to predictions of vehicle effects on the dermal absorption of similar compounds. Although these studies were conducted in porcine skin, the results are relevant to human dermal absorption due to the histological and biochemical similarity of human and porcine skin (Reifenrath et al 1984; Monteiro-Riviere 1986).

The stratum corneum was processed using trypsin, heat and desiccation. Some alterations in the straum corneum environment can be expected due to the processing procedures, such as removal of free water and changes in keratinocyte protein structure. Stratum corneum partitioning of lipophilic compounds in trypsinized, dried human stratum corneum was shown by (Raykar et al 1988) to be correlated with partitioning into extracted stratum corneum lipids. If the stratum corneum lipids are assumed to be the primary route of absorption through the stratum corneum, then partitioning into stratum corneum lipids is of interest. Differences in the effects of solvents in isolated stratum corneum compared to hydrated, intact stratum corneum may be due to variations in the extent of solvent penetration. Assuming that solvent effects on partitioning in isolated stratum corneum are quantitatively the same as in intact stratum corneum may not be valid. However, it is reasonable to assume that the differences would be largely in extent, while the overall pattern remains similar. This hypothesis is supported by the data of the present study.

Assuming that a solvent and non-electrolyte solute do not react chemically with each other, the solubility of a solute in a solvent or chemical mixture is a function of the change in enthalpy and entropy when the solute dissolves. The total energy required for overcoming the solvent intermolecular bonds and the energy released upon association of the solute molecules with the solvent determines the change in enthalpy whereas change in

entropy is determined by the amount of disorder introduced to the system (Atkins 1994). Since systems tend towards lower energy (Atkins 1994), change in enthalpy and entropy will determine the solute partitioning between the solvents at equilibrium. According to this hypothesis, the changes in partitioning patterns observed when SLS is added to the solvent should be influenced by the effects of SLS on intermolecular forces. Water exhibits relatively strong intermolecular attraction due to charge interactions and H-bonding. Non-polar compounds are not attracted strongly to water molecules and therefore do not overcome the intermolecular bonds between water molecules readily. Lipids in the stratum corneum, however, contain long carbon chains that can attract non-polar molecules through the action of London dispersion forces. The energy of the system will therefore be balanced, at equilibrium, when non-polar solutes are present at higher concentrations in the stratum corneum lipids than in water. The difference in concentration should be correlated with lipophilicity, expressed as log Ko/w. This hypothesis is supported by the data presented in Figure 1, which shows an increased partitioning into the stratum corneum from water as the log Ko/w of the solute increases. SLS, when present at concentrations above the CMC, causes the formation of micelles around the non-polar solute molecules. The concentration of SLS used in this study was well above the CMC, which is ca. 0.23% (m/v) (Mukerjee & Mysels 1971). The polar region of the surfactant is strongly attracted to water due to charge interactions, which maintains a favorable energy balance in the system, at equilibrium, when solute is present in the solvent at relatively high concentrations. The lipophilicity of the solute is therefore expected to have a weaker influence on its partitioning when SLS is added to the system due to increased lipophilicity in the solvent as shown in Figure 1.

The hypothesis presented above is also supported by the partitioning behavior of the tested compounds in ethanol. Ethanol contains a short carbon chain and a polar group, which allows ethanol to attract polar and non-polar molecules. The addition of SLS, therefore, did not substantially change the partitioning behavior of solutes across a range of lipophilicity (Figure 2). There was, however, still a weak correlation between partitioning into stratum corneum and lipophilicity, which indicates that the stratum corneum has a higher lipophilicity than ethanol.

Propylene glycol mixed with SLS slowly solidifies into a paste-like consistency at room temperature. Trapping of solute in the solidified solvent before partitioning reached equilibrium explains the lowered partitioning from propylene glycol when SLS was added (Figure 3). Similar to partitioning from ethanol, weak correlation between lipophilicity and stratum corneum partitioning was found, indicating that the stratum corneum has a higher lipophilicity than propylene glycol.

In the present study, permeability showed large inter-compound variability compared to partitioning; and permeability was not related to compound lipophilicity and stratum corneum partitioning across all solvent systems (Figure 5, Figure 6 and Figure 7). Although partitioning is essential for dermal absorption, permeability is influenced by the diffusivity of a compound in the stratum corneum lipids and the pathway length. The relationship between partitioning, diffusivity and pathway length allows qualitative deductions to be made from comparisons between partitioning and permeability data. Since the pathway length was unchanged between permeability estimations in the same solvent system and partitioning was not correlated with permeability within solvents systems, it can be concluded that the physical and chemical factors that predict partitioning do not predict diffusivity.

The addition of SLS to ethanol generally increased permeability, while partitioning from ethanol was largely unaffected by SLS. It suggests that the effect of SLS on permeability from ethanol is largely due to an effect on diffusivity. This effect may be related to the addition of water with the SLS rather than an effect of SLS itself. Binary mixtures of water and ethanol have been shown to increase dermal absorption compared to pure ethanol. Pure ethanol dehydrates the stratum corneum, which normally decreases permeability. With the addition of water, however, ethanol may have a disruptive effect on stratum corneum lipid structure causing increased permeability. Other suggested mechanisms include effects on the putative pore pathway, increased solubility in stratum corneum lipids and ethanol copermeation (Berner et al 1989; Kurihara-Bergstrom et al 1990; Megrab et al 1995; Kim et al 1996; Levang et al 1999; Panchagnula et al 2001).

SLS generally decreased permeability and partitioning from water when compared to permeability from pure water, with the effect on partitioning increasing with an increase in compound lipophilicity. Phenol, which did

not show a significant change in permeability, is the compound in the group with the lowest lipophilicity. Phenol partitioning was also not significantly changed by the addition of SLS (Table 1). Although this suggests that the lack of effect of SLS on phenol permeability and partitioning from water may be related, there is no consistent correlation between permeability and partitioning in the other compounds and it is possible that a small SLS effect could be masked by experimental variability. If only the direction of effect is considered, however, the similarity of SLS effects on partitioning and permeability from water suggests that the effect on partitioning is related to the effect on permeability and that the relationship is strong enough not to be completely masked by differences in diffusivity. From a practical perspective the data suggests that washing contaminated skin using water and a surfactant should, apart from removing some of the contaminating chemical, reduce absorption when compared to washing in water without a surfactant. However, should the surfactant induce skin irritation, as might be expected in an in vivo situation, this physicochemical advantage may be reduced.

Pure propylene glycol dehydrates the stratum corneum, which decreases permeability. A 66% aqueous solution of propylene glycol, however, enhances permeability (Panchagnula et al 2001). Proposed mechanisms of absorption enhancement include a cosolvency effect (Barry 1983) and a carrier mechanism (Hoelgaard & Mollgaard 1985). In the present study, the influence of SLS on permeability from propylene glycol was not consistent, although partitioning was generally reduced (Figure 3 and Figure 4; Table 2). Since SLS was added to propylene glycol in the form of an aqueous solution, the influence of water was confounded with the influence of SLS. SLS is not soluble in pure propylene glycol. An aqueous mixture of propylene glycol and SLS therefore resembles more probable real-world exposures to this mixture. An example is when an aqueous solution of SLS is used as a cleaning agent after dermal exposure to a chemical in propylene glycol. The addition of SLS diminished the dehydrating effect of propylene glycol, weakening the decrease in permeability associated with pure propylene glycol and opening up the possibility of absorption enhancement through one or both mechanisms mentioned above.

Models of dermal absorption usually assume permeability to be a first order process. However, changes in the stratum corneum lipid environment induced by solutes and solvent components may be non-linear over time

and concentration (Berner et al 1989; Kurihara-Bergstrom et al 1990; Megrab et al 1995; Kim et al 1996; Levang et al 1999; Panchagnula et al 2001). The stratum corneum lipids include long chain ceramides, fatty acids, cholesterol and triglycerides (Monteiro-Riviere et al 2001), which form parallel lamellae on corneocyte surfaces. Inside the lamellae, the lipids are arranged in bilayers of ordered, crystalline phases bordering a central band of fluid lipids. The bilayer arrangement of the lipids results in continuous bands of polar layers and non-polar layers (Bouwstra et al 2003). Differences in lipid composition and structure occur between deep and superficial layers and on different body areas (Monteiro-Riviere 1986; Bouwstra et al 2003). The complexity of this system allows for the possibility of a variety of interactions and solvent effects on partitioning and diffusivity, as demonstrated by the present study. Caution should therefore be used when attempting to use data obtained from a particular solvent system to predict parameters in a different solvent system.

This study related the partitioning of parent compound into isolated stratum corneum to the absorption of total C-14 through dermatomed skin. The absorption of C-14 reflected the driving concentration of parent compound for diffusion across the stratum corneum. It allowed the estimation of total absorption of the C-14 labeled compound in an experimental system where metabolism may or may not be significant. The absorption/time curve is, according to Fick's law of diffusion, a reflection of the permeant concentration gradient, permeant partitioning, permeant diffusivity and pathway length, which is related to the membrane thickness in a flow-through cell. Metabolism of parent compound in the viable epidermis may alter subsequent partitioning between the viable epidermis and the receptor fluid and could influence the shape of the absorption/time curve. Although the assumption cannot be made that the initial partitioning step in absorption is the overriding determinant of absorption, this first step in the disposition of parent drug across the stratum corneum is generally assumed to be rate-limiting and must be understood before any subsequent metabolism of penetrated parent drug can be taken into account. The approach used in this study revealed generally repeatable solvent influences on absorption across a range of compounds (Figure 4) that could be related to independently estimated solvent/stratum corneum partitioning. However, it provides a limited description of the nature of parent compound absorption into the systemic circulation due to the possible influences of permeant metabolism in the epidermis and dermis. This limitation must be considered when conclusions are drawn from the absorption data relative to the risk of systemic toxicity. These data apply to assessing vehicle and surfactant effects on the first step in dermal

absorption–partitioning into the stratum corneum. The use of chromatographic techniques and, ideally, perfused skin models (Riviere et al 1986) are needed to fully elucidate the effects of metabolism on a dermal absorption profile.

It was concluded that, for the compounds tested, partitioning into the stratum corneum was determined by the relative solubility of the solute in the donor solvent and the stratum corneum lipids. Permeability, however, reflected the result of successive, complex processes and is not always predictable from stratum corneum partitioning. This finding has considerable significance on the use of partition coefficients alone, determined from neat chemical exposure, to estimate chemical absorption for mixture exposures. Physical–chemical interactions present within the exposure mixture should be defined before partition coefficients are employed in risk assessment models.

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Table 1. Estimated log P stratum corneum/solvent values in water, water plus sodium lauryl sulphate (SLS), ethanol (EtOH), ethanol plus SLS, propylene glycol (PG) and PG plus SLS with standard errors (SE) (n=5) and log P octanol/water (log P o/w) values (Howard and Meylan 1997) for phenol (PHE), p-nitrophenol (PNP), simazine (SIM), atrazine (ATR), methyl parathion (MPA), propazine (PRO), ethyl parathion (EPA), fenthion

	Log	Water				EtOH						PG +	
	Po/w	Water	SE	+ SLS	SE	EtOH	SE	+ SLS	SE	PG	SE	SLS	SE
PHE	1.46	1.081	0.037	1.166	0.025	0.556	0.048	0.500	0.038	0.689	0.097	0.695	0.071
PNP	1.91	1.246	0.021	1.215	0.024	0.633	0.110	0.658	0.073	0.878	0.240	0.455	0.050
SIM	2.18	0.737	0.025	1.313	0.029	0.773	0.008	0.932	0.027	0.784	0.052	0.992	0.062
ATR	2.61	1.722	0.113	1.206	0.022	0.775	0.045	0.604	0.104	1.256	0.094	0.623	0.046
MPA	2.86	1.922	0.078	1.370	0.037	0.733	0.054	0.770	0.037	1.369	0.067	0.856	0.049
PRO	2.93	1.969	0.381	1.210	0.070	0.797	0.064	0.738	0.050	0.992	0.160	0.652	0.036
EPA	3.83	2.952	0.065	1.114	0.074	0.983	0.037	0.760	0.088	1.100	0.226	0.979	0.023
FEN	4.09	3.006	0.036	1.279	0.209	0.693	0.058	0.763	0.033	0.892	0.052	0.767	0.115
CPY	4.96	3.784	0.710	1.417	0.031	0.853	0.066	0.787	0.033	1.241	0.034	0.974	0.044
PCP	5.12	2.534	0.189	1.305	0.094	0.897	0.094	1.189	0.144	1.402	0.056	1.120	0.037

(FEN), chlorpyrifos (CPY) and pentachlorophenol (PCP).

Table 2. Estimated permeability values (cm/h) from water, water plus sodium lauryl sulphate (SLS), ethanol (EtOH), ethanol plus SLS, propylene glycol (PG) and PG plus SLS with standard errors (SE) (n=5) for phenol (PHE), p-nitrophenol (PNP), simazine (SIM), atrazine (ATR), methyl parathion (MPA), propazine (PRO), ethyl parathion (EPA), fenthion (FEN), chlorpyrifos (CPY) and pentachlorophenol (PCP).

	Water	SE	Water + SLS	SE	EtOH	SE	EtOH + SLS	SE	PG	SE	PG + SLS	SE
PHE	4.377	0.194	4.380	0.234	4.210	0.291	4.444	0.238	0.127	0.012	0.179	0.015
PNP	2.222	0.344	1.755	0.089	0.350	0.018	1.604	0.074	0.013	0.001	0.030	0.009
SIM	0.484	0.061	0.199	0.039	0.095	0.014	0.355	0.030	0.023	0.002	0.062	0.041
ATR	1.126	0.221	0.703	0.120	0.068	0.002	0.606	0.031	0.035	0.019	0.027	0.005
MPA	4.918	0.634	0.634	0.068	0.178	0.021	0.712	0.052	0.049	0.005	0.036	0.010
PRO	0.233	0.013	0.144	0.028	0.032	0.007	0.093	0.010	0.008	0.002	0.008	0.002
EPA	0.410	0.049	0.236	0.043	0.157	0.032	0.122	0.009	0.035	0.004	0.042	0.023
FEN	0.463	0.013	0.195	0.033	0.102	0.007	0.256	0.042	0.015	0.002	0.027	0.002
CPY	0.061	0.018	0.052	0.013	0.013	0.002	0.036	0.003	0.007	0.001	0.008	0.002
PCP	1.648	0.217	0.393	0.040	0.078	0.020	0.297	0.077	0.013	0.002	0.016	0.003

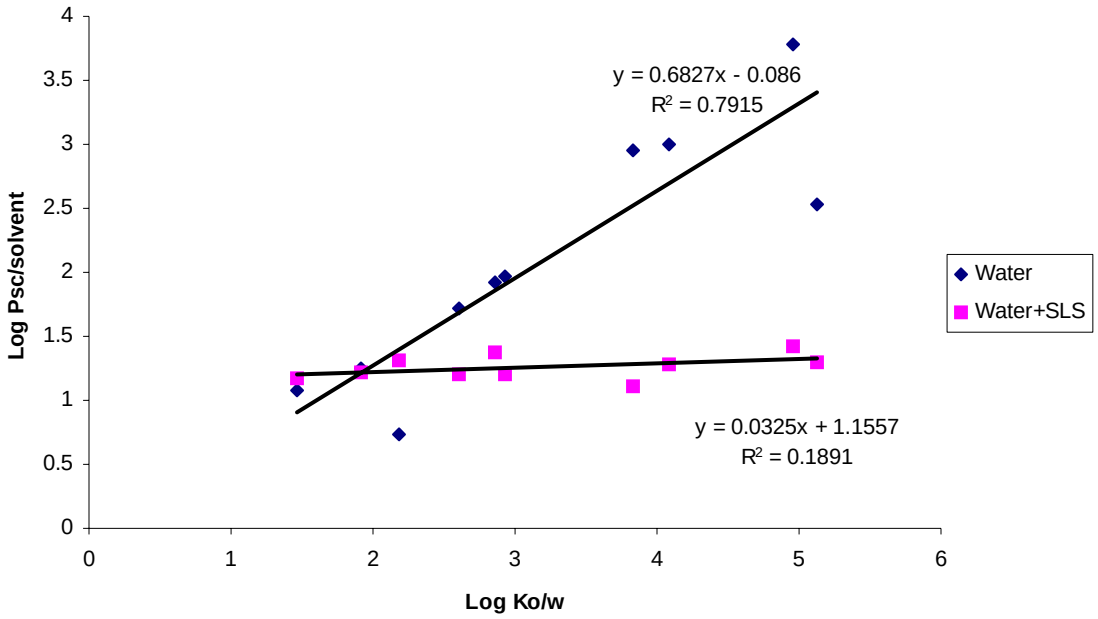

Figure 1. Log Ko/w plotted against the mean log partitioning of stratum corneum/solvent from water and water with sodium lauryl sulphate. Compounds represented are, from left to right, phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol. The linear regression lines, regression equations and R^2 values of the plot for each solvent is displayed (n = 5).

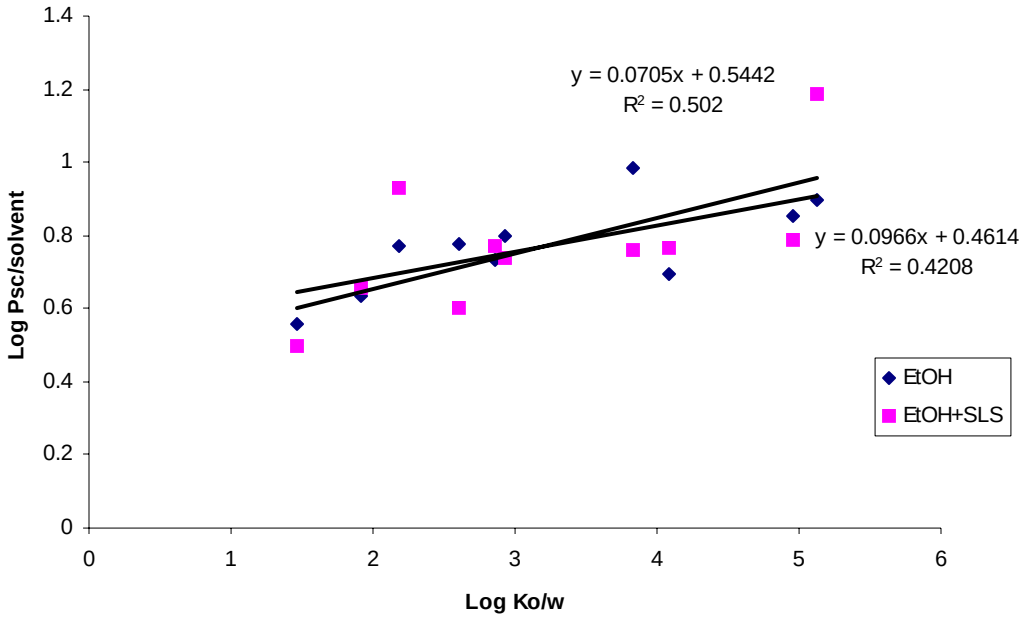

Figure 2. Log Ko/w plotted against the mean log partitioning of stratum corneum/solvent from ethanol and ethanol with sodium lauryl sulphate. Compounds represented are, from left to right, phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol. The linear regression lines, regression equations and R^2 values of the plot for each solvent is displayed (n = 5).

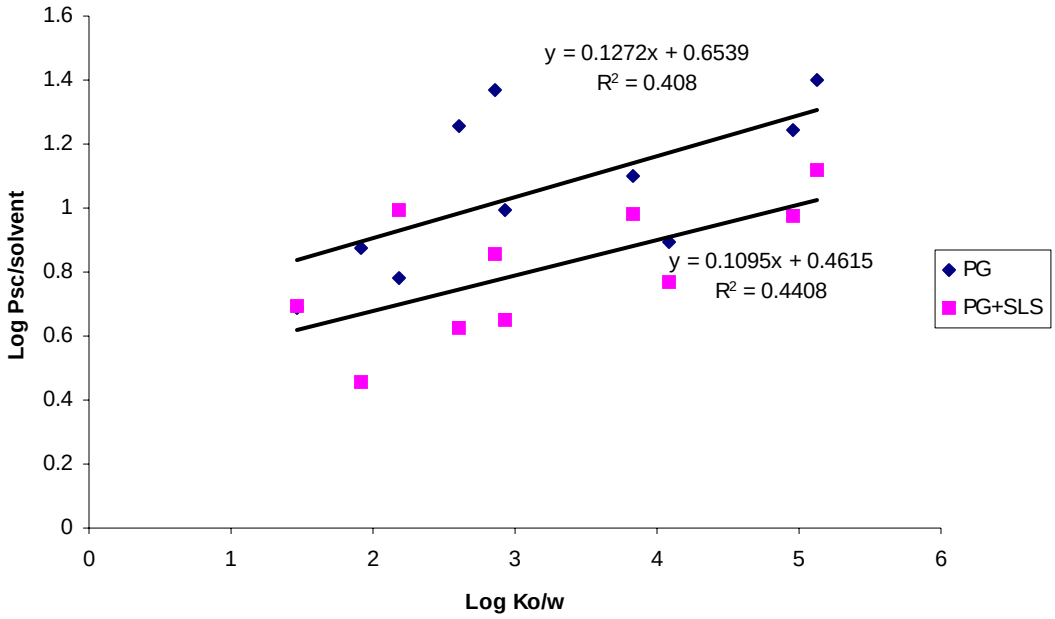

Figure 3. Log Ko/w plotted against the mean log partitioning of stratum corneum/solvent from propylene glycol and propylene glycol with sodium lauryl sulphate. Compounds represented are, from left to right, phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol. The linear regression lines, regression equations and R^2 values of the plot for each solvent is displayed (n = 5).

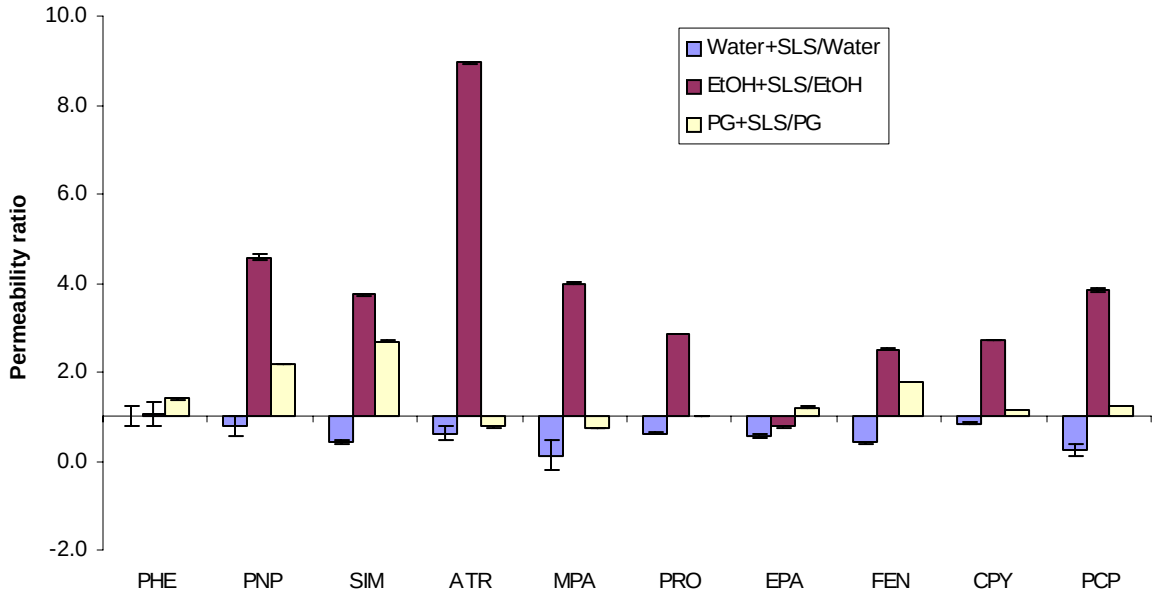

Figure 4. The permeability ratios of mean permeability from water with sodium lauryl sulphate (SLS)/water, ethanol with SLS/ethanol and propylene glycol with SLS/propylene glycol of phenol (PHE), p-nitrophenol (PNP), simazine (SIM), atrazine (ATR), methyl parathion (MPA), propazine (PRO), ethyl parathion (EPA), fenthion (FEN), chlorpyrifos (CPY) and pentachlorophenol (PCP). Error bars denote the average standard error of the means comprising the ratio (n = 5).

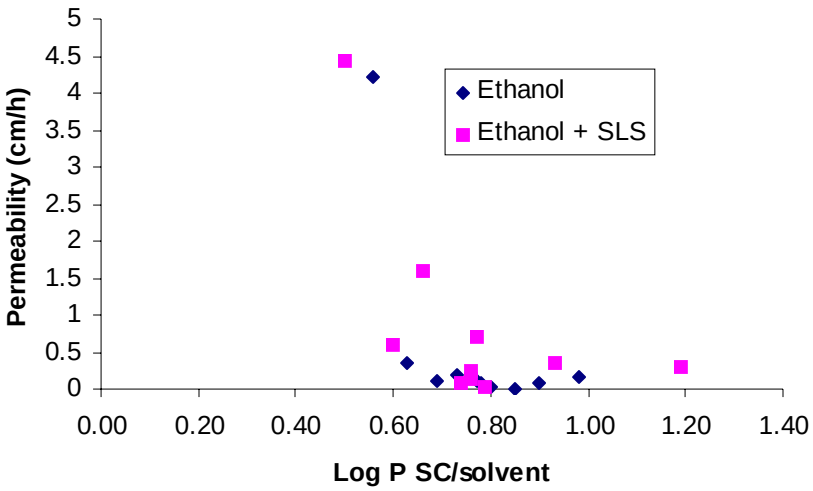

Figure 5. Scatterplot to compare mean values of permeability (n=4) and log stratum corneum (SC)/solvent partitioning (n=5) from ethanol and ethanol plus sodium lauryl sulphate for phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol.

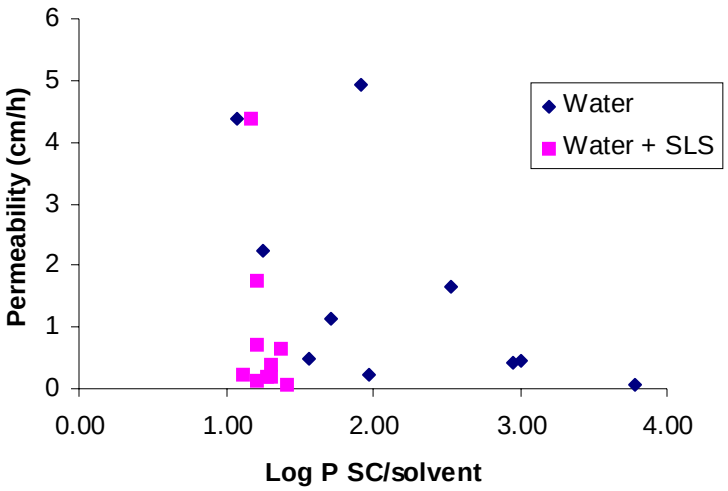

Figure 6. Scatterplot to compare mean values of permeability (n=4) and log stratum corneum (SC)/solvent partitioning (n=5) from water and water plus sodium lauryl sulphate for phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol.

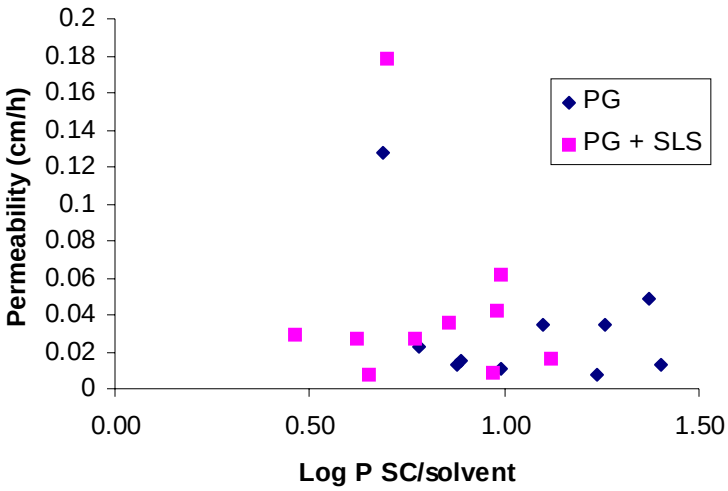

Figure 7. Scatterplot to compare mean values of permeability (n=4) and log stratum corneum (SC)/solvent partitioning (n=5) from propylene glycol (PG) and PG plus sodium lauryl sulphate for phenol, p-nitrophenol, simazine, atrazine, methyl parathion, propazine, ethyl parathion, fenthion, chlorpyrifos and pentachlorophenol.

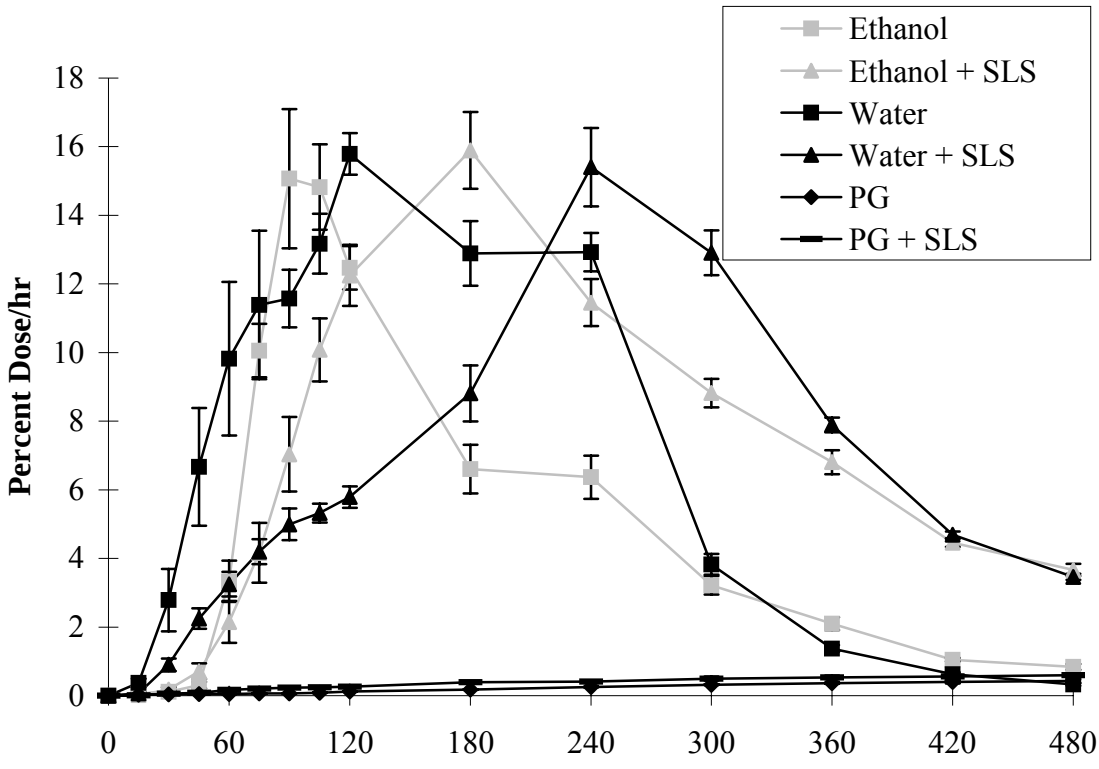

Figure 8. Flow-through cell estimated flux/time curves for phenol from ethanol, ethanol plus sodium lauryl sulphate (SLS), water, water plus SLS, propylene glycol (PG) and PG plus SLS. Error bars denote standard errors (n=5).